UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/109,119	06/30/1998	BENJAMIN W. BOLDT	GTIBEN.001	3198

7590 07/22/2002

MARK K JOHNSON
P O BOX 510644
NEW BERLIN, WI 531310644

EXAMINER
GOLDBERG, JEANINE ANNE

ART UNIT	PAPER NUMBER
1634	22

DATE MAILED: 07/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/109,119	BOLDT ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5 and 7-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5 and 7-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). *20* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed May 29, 2002.

2. Currently, claims 1, 3-5, 7-16 are pending. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow.

3. Any objections and rejections not reiterated below are hereby withdrawn.

4. This action contains new grounds of rejection necessitated by amendment.

New Grounds of Rejection Necessitated by Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A3) Claims 1-16 are rejected over the recitation "between the primers". Claim 1 and 13 are directed to only using a single primer, therefore, "between the primers" appears to lack antecedent basis.

B3) Claims 1-16 refer to "capturing the amplified sequence". Based upon the rejection above, since the claim does not have antecedent basis for two primers, the instant rejection is applied if the phrase were to be deleted. It is unclear whether the probes that hybridize to the amplified sequence capture the primer template sequence or the extension product. The claims as written appear to read upon capturing the

nucleic acid which was amplified which may be done by either capturing the primer template sequence or the extension product. As provided in the interview of April 19, 2001, the applicants explained that the instant invention is directed to capturing the extended region, not the amplified sequence as a whole. Therefore, a clarification that the claims are directed to probing for the extended sequence is requested.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1, 3-5, 7-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Newton et al (US Pat. 5,595,890, January 1997) in view of Monforte et al. (US Pat. 5,830,655, November 1998) and Day et al (Laboratory Methods for the detection of mutations and polymorphisms in DNA, Chapter 26, pages 287-290, 1997).

Newton et al. (herein referred to as Newton) teaches a method for testing genomic DNA to determine if at least one base is present by making a solution comprising genomic DNA, adding a primer which hybridizes to a targeted section of the genomic DNA, wherein the primer 3' nucleotide will hybridize and extend along the genomic DNA if the base is present, mixing DNA polymerase into the solution, amplifying the genomic DNA if the base at the 3' end of the primer hybridizes and detecting the amplified polynucleotide. Specifically, Newton teaches treating a sample

with nucleoside triphosphates, an agent for polymerization, a diagnostic primer for a diagnostic portion of a target base sequence such that the primer is either complementary to the suspected variant nucleotide or to the corresponding normal nucleotide (limitations of Claim 1a, b, c, d, f). Newton teaches where the terminal nucleotides of the diagnostic primer is complementary to the corresponding nucleotide in the target base sequence an extension product of the diagnostic primer is synthesized; and no extension product is synthesized when the terminal nucleotide of the diagnostic primer is not complementary to the corresponding nucleotide in the target base sequence (col. 3, lines 10-30). Newton teaches that detecting the presence or absence of the suspected variant nucleotide from the presence or absence of an extension product (col. 3, lines 28-30). Newton teaches that any extension product formed may be detected in any form, such as single or double-stranded form (limitations of Claim 3). Newton teaches that the template and the primer extension product may be separated under denaturing conditions (col. 4, lines 15-16). Newton teaches that "if only 1, 2, or 3 nucleoside triphosphates are present then the diagnostic primer will only extend as far as the presence of these nucleoside triphosphates will permit (col. 7, lines 60-68). Newton teaches that one or more of the nucleoside triphosphates present in the reaction mixture may be labeled or marked in any convenient manner, e.g. fluorescently labeled (col. 8, lines 15-20)(limitations of Claim 8, 9). Newton teaches that "as the size of the sum of the sizes of the diagnostic primers increases, so amplification products can be resolved, for example on agarose gels (col. 22, lines 38-42). Newton teaches that his method meets the need for "a simple method for directly detecting at least one

single base difference in nucleic acids such as genomic DNA in which detection steps are minimized resulting in a method which may be performed quickly, accurately and easily with minimal operator skill" (col. 2, lines 62-65).

Newton does not specifically teach capturing the extended polynucleotides using probes which are complementary to the extension product.

However, Monforte teaches amplification using primers and subsequent detection of the size of an extension product. Monforte teaches the extension segment can be immobilized by attachment to a solid support. Monforte teaches that the probes for immobilization may be located in the primer region, or "alternatively, if a portion of the sequence of the extension product is known, the immobilization attachment site may be contained within a region of the extension segment" (col. 7, lines 15-18)(limitations of Claim 1 d). Monfote teaches coated plates such as those available from Pierce may be used to immobilize the modified oligonucleotides (col. 30, lines 41-45). Monforte teaches that biotinylated oligonucleotides may be used in immobilization to streptavidin or avidin-coated solid supports (col. 30, lines 5556, Ex. 2A)(limitations of Claims 11, 12). Monforte teaches a list of solid support material which may be used for the detection of the nucleic acids (col. 27-28). Monforte teaches that denaturing may be performed using heat or chemical denaturant (col. 27, lines 24-26)(limitations of claims 4, 5, 15).

Moreover, Day teaches gel detection using electrophoresis is "manual and time-consuming and therefore, also expensive" (page 289). Day teaches it would seem obvious therefore, to aim to avoid electrophoresis for all mutation analysis when studying composition of sequence. Day teaches that "almost invariably, the first step in

analytical molecular genetics is PCR amplification of the regions of interest: the second step is often either a capture-binding assay or an electrophoretic assay (page 289, para 1). Day teaches the benefits of using the 96-well microtiter plates (limitations of Claim 7). Day teaches that the 8x 12 arrays may be a solid-phase coated plastic. The benefits of the microtiter plate include the ability to automate pipetting and other manipulations, the compact nature of the array and the lack of need to label and store tubes in racks.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the nucleic acid detection method of Newton which amplifies regions of interest using primers with 3' nucleotides of interest to detect extension products with the teachings of Monforte for detecting extension products using solid support immobilization to the extension segment region. The ordinary artisan would have been motivated to detect the presence of an extension product as taught by Newton. Rather than using detection by gel visualization, the ordinary artisan would have been motivated to have detected the presence of an extension product using a solid support, wherein the solid support contains probes directed to the extension product, as taught by Monforte. The ordinary artisan, as taught by Day, would be motivated to have used a solid support in lieu of gel detection because gel detection using electrophoresis is "manual and time-consuming and therefore, also expensive". Therefore, modifying the method of Newton which uses gel electrophoresis for detection of extension products, the ordinary artisan given the well known drawbacks of electrophoretic detection would have been motivated to have detected the extension

products using another means. As taught by Day, the detection is often either by a capture-binding assay or an electrophoretic assay. The ordinary artisan would have been motivated to have designed an assay which utilized the more preferable capture binding assay for determining the composition of a sequence by using capture probes specifically designed to be complementary to the extension product, as taught by Monforte. Detection of the extension product by capturing the extension product on a solid support would have been a preferable means of detecting an extension product over the gel electrophoretic method of Newton.

Conclusion

7. No claims allowable over the art.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of formal matters can be directed to the patent analyst, Pauline Farrier, whose telephone number is (703) 305-3550.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J. Goldberg

Jeanine Goldberg
July 16, 2002

Lisa B. Arthur

LISA B. ARTHUR
PRIMARY EXAMINER
GROUP ~~1800~~ 1600